

all assays, not just PCR, as applicant states (see introduction, column 2)...Loakes et al. does not teach the use of these primers in an array.

With respect to Chetverin et al., the Examiner argues:

Chetverin et al. does teach the advantages of linking sets of oligonucleotide probes to solid supports. These arrays have use for sequencing of genomic DNA or other large target sequences.

In combining Loakes et al. with Chetverin et al., the Examiner argues:

Thus it is maintained that it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the universal bases of Loakes et al. in probes on an array, as taught by Chetverin et al. One would have been motivated to want to use the universal nucleotides disclosed by Loakes et al. in light of their universal pairing ability and their limited interference in the hybridization of an oligonucleotide with its target sequence.

Applicants disagree with this rejection under 35 U.S.C. § 103(a). In order to make a prima facie obviousness rejection, the Examiner must show, among other things: (1) that one of ordinary skill in the art would have been motivated to combine the teachings of the cited references; and (2) that in combining the teachings, one of skill in the art would have had a reasonable expectation of success in practicing the invention.

As noted in *In re Napier*, 55 F.3d 610 (Fed. Cir. 1995), "Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination." A similar point was made in *In re Laskowski*, 871 F.2d 115 (Fed. Cir. 1989), "The mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification" (quoting *In re Gordon*, 733 F.2d 900 (Fed. Cir. 1984)).

As noted in *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991), "a proper analysis under § 103 requires, inter alia, consideration of...whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success."

Applicants maintain that the Examiner has failed to establish that one of skill in the art would have had motivation to combine the probes of Loakes et al. with the nucleotide arrays of Chetverin et al. Furthermore, even if one made an array of gapped probes at the time of filing, the Examiner has not cited any teachings as to how one of ordinary skill in the art would have

used such an array to perform any useful task. Accordingly, the art does not provide any reasonable expectation of success.

Applicants assert that Loakes et al. does not provide motivation to combine the gapped probes of Loakes with the arrays of Chetverin. Applicants disagree with the Examiner's statement that: "clearly Loakes et al. intended for the universal bases to have use in all assays". At page 2361, Loakes et al. states: "To be of routine use in recombinant DNA experiments the modified oligonucleotides *must be able to prime DNA polymerases.*" (*emphasis added*). Later in the same paragraph, Loakes et al. state that "when used in the polymerase chain reaction the modified base(s) *must be able to act as a template for the incorporation of a base* for the amplification to proceed." (*emphasis added*). And in a related statement in the same paragraph, Loakes et al. state: "This ability [presumably the ability to be a template for incorporation of a base by a polymerase] *is required* if oligonucleotides containing such abnormal bases are to be applied to reduction of primer multiplicity, nucleotide sequencing, polymerase chain reaction (PCR) and site-directed mutagenesis." (*emphasis added*). Applicants assert that these statements by Loakes et al. only suggest the use of gapped probes for applications that employ a DNA polymerase or for "recombinant DNA experiments". Even the comment relating to sequencing is clearly in a context showing that Loakes et al. contemplates only sequencing based on DNA polymerase activity (e.g. Sanger sequencing) and not sequencing by hybridization. Accordingly, Loakes et al. provide no teaching or suggestion that the gapped probes disclosed therein could be used for making an array or for a probe set comprising multiple instances of a probe.

Applicants assert that Chetverin also fails to provide any motivation to use gapped probes in the arrays disclosed therein. Applicants are unable to find anywhere in Chetverin any reference to the use of a gapped probe. Applicants note that the Examiner has also failed to cite any reference to use of a gapped probe in Chetverin.

Therefore, there is no motivation in either Chetverin or Loakes to combine a gapped probe with an array. Furthermore, Applicants assert that, as of the time of filing, there was no understanding in the art of how a set of gapped probes could be used to, for example, elucidate the sequence of a nucleic acid. None of the references cited in this prosecution teach how to deduce sequence information from hybridization to a set of gapped probes. Accordingly, motivation to combine the gapped probes with arrays could not be supplied by the knowledge of

one of ordinary skill in the art. Given that motivation to combine is not present in the cited art and could not have been part of the general knowledge of one of skill in the art, Applicants assert that the Examiner has failed to provide a motivation to combine Loakes et al. with Chetverin et al.

Even if one were to assume, *in arguendo*, that there was motivation to combine these references, the obviousness rejection still fails because one of ordinary skill in the art would not have had a reasonable expectation of success to do anything useful (e.g. sequencing) with an array of gapped probes. As asserted above, at the time of filing, there was no information in the art about how one would extract useful information from the hybridization of a nucleic acid to an array of gapped probes.

Because the Examiner has failed to provide a motivation to combine the cited references, and because the Examiner has failed to indicate teachings that would provide one of ordinary skill in the art with a reasonable expectation of success in using the teachings of the combined references, Applicants assert that the Examiner has failed to make a proper prima facie case of obviousness.

Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103.

### Conclusion

For the reasons given above, Applicants respectfully request reconsideration of this application and timely allowance of the pending claims. Applicants submit that the pending claims, as amended, are in condition for allowance. If the Examiner believes that a personal or telephonic interview would expedite allowance of these claims, he is invited to call the undersigned.

If there are any fees, such as excess claims fees, due in connection with the filing of this Response, please charge the fees to our Deposit Account No. 06-1448. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

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